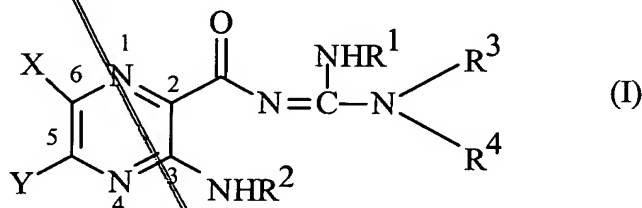


Claims:

1. A compound represented by formula (I):



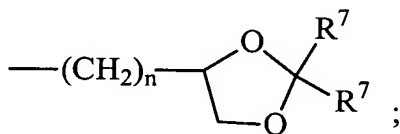
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or -N(R²)₂;

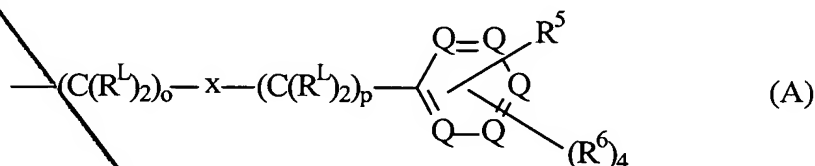
R¹ is hydrogen or lower alkyl;

each R² is, independently, -R⁷, -(CH₂)_m-OR⁸, -(CH₂)_m-NR⁷R¹⁰, -(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰, -(CH₂)_n-Z_g-R⁷, -(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂)_n-CO₂R⁷, or



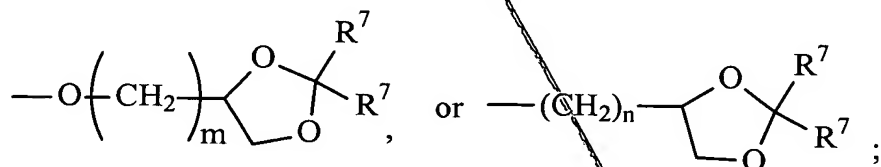
R³ and R⁴ are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower (alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or

pyridyl- lower alkyl, with the proviso that at least one of R³ and R⁴ is a group represented by formula (A):



wherein

each R^L is, independently, -R⁷, -(CH₂)_n-OR⁸, -O-(CH₂)_m-OR⁸,
 -(CH₂)_n-NR⁷R¹⁰, -O-(CH₂)_m-NR⁷R¹⁰, -(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -O-(CH₂)_m(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂CH₂O)_m-R⁸,
 -O-(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰,
 -O-(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰,
 -O-(CH₂)_m-C(=O)NR⁷R¹⁰, -(CH₂)_n-(Z)_g-R⁷, -O-(CH₂)_m-(Z)_g-R⁷,
 -(CH₂)_n-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -O-(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -(CH₂)_n-CO₂R⁷, -O-(CH₂)_m-CO₂R⁷, -OSO₃H, -O-glucuronide, -O-glucose,



each o is, independently, an integer from 0 to 10;

each p is an integer from 0 to 10;

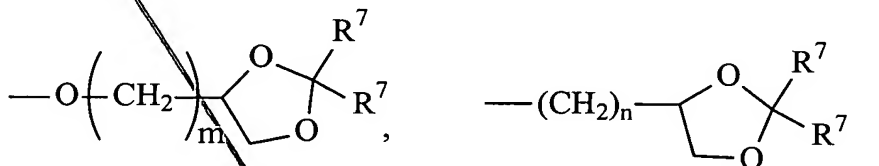
with the proviso that the sum of o and p in each contiguous chain is from 1 to 10;

each x is, independently, O, NR¹⁰, C(=O), CHOH, C(=N-R¹⁰), CHNR⁷R¹⁰, or represents a single bond;

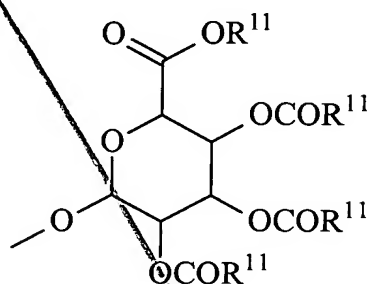
each R⁵ is, independently, -(CH₂)_m-OR⁸, -O-(CH₂)_m-OR⁸,
 -(CH₂)_n-NR⁷R¹⁰, -O-(CH₂)_m-NR⁷R¹⁰, -(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -O-(CH₂)_m(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂CH₂O)_m-R⁸,

a
cont

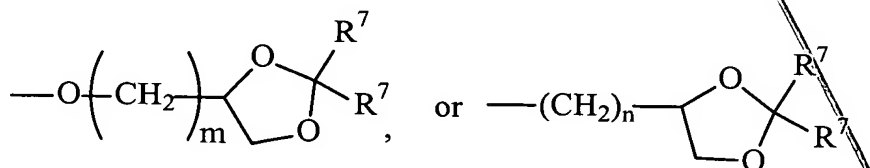
-O-(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰,
 -O-(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰,
 -O-(CH₂)_m-C(=O)NR⁷R¹⁰, -(CH₂)_n-(Z)_g-R⁷, -O-(CH₂)_m-(Z)_g-R⁷,
 -(CH₂)_n-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -O-(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -(CH₂)_n-CO₂R⁷, -O-(CH₂)_m-CO₂R⁷, -OSO₃H, -O-glucuronide, -O-glucose,



or



each R⁶ is, independently, -R⁷, -OR¹¹, -N(R⁷)₂, -(CH₂)_m-OR⁸,
 -O-(CH₂)_m-OR⁸, -(CH₂)_n-NR⁷R¹⁰, -O-(CH₂)_m-NR⁷R¹⁰,
 -(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -O-(CH₂)_m(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -(CH₂CH₂O)_m-R⁸, -O-(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰,
 -O-(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰,
 -O-(CH₂)_m-C(=O)NR⁷R¹⁰, -(CH₂)_n-(Z)_g-R⁷, -O-(CH₂)_m-(Z)_g-R⁷,
 -(CH₂)_n-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -O-(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸,
 -(CH₂)_n-CO₂R⁷, -O-(CH₂)_m-CO₂R⁷, -OSO₃H, -O-glucuronide, -O-glucose,

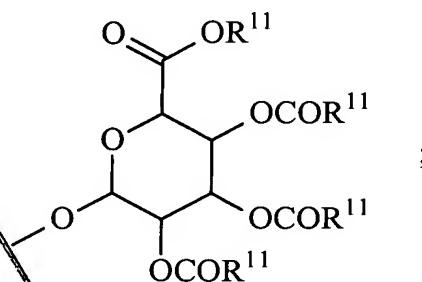


wherein when two R⁶ are -OR¹¹ and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two R⁶ may be bonded together to form a methylenedioxy

group;

each R^7 is, independently, hydrogen or lower alkyl;

each R^8 is, independently, hydrogen, lower alkyl, $-C(=O)-R^{11}$, glucuronide, 2-tetrahydropyranyl, or



each R^9 is, independently, $-CO_2R^7$, $-CON(R^7)_2$, $-SO_2CH_3$, or $-C(=O)R^7$;

each R^{10} is, independently, $-H$, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, or $-CH_2-(CHOH)_n-CH_2OH$;

each Z is, independently, $CHOH$, $C(=O)$, $CHNR^7R^{10}$, $C=NR^{10}$, or NR^{10} ;

each R^{11} is, independently, lower alkyl;

each g is, independently, an integer from 1 to 6;

each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

each Q is, independently, $C-R^5$, $C-R^6$, or a nitrogen atom, wherein at most three Q in a ring are nitrogen atoms;

or a pharmaceutically acceptable salt thereof, and

inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

2. The compound of Claim 1, wherein Y is $-NH_2$.
3. The compound of Claim 2, wherein R^2 is hydrogen.
4. The compound of Claim 3, wherein R^1 is hydrogen.
5. The compound of Claim 4, wherein X is chlorine.

6. The compound of Claim 5, wherein R^3 is hydrogen.

7. The compound of Claim 6, wherein each R^L is hydrogen.

8. The compound of Claim 7, wherein o is 4.

9. The compound of Claim 8, wherein p is 0.

10. The compound of Claim 9, wherein x represents a single bond.

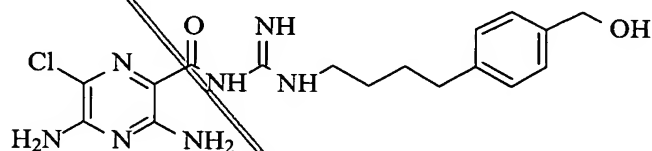
11. The compound of Claim 10, wherein each R^6 is hydrogen.

12. The compound of Claim 11, wherein at most one Q is a nitrogen atom.

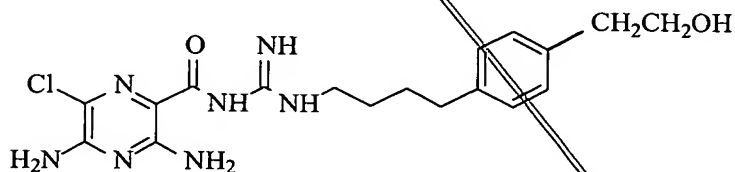
13. The compound of Claim 12, wherein no Q is a nitrogen atom.

14. The compound of Claim 13, wherein R^5 is $-(CH_2)_m-OR^8$.

15. The compound of Claim 14, which is represented by the formula:

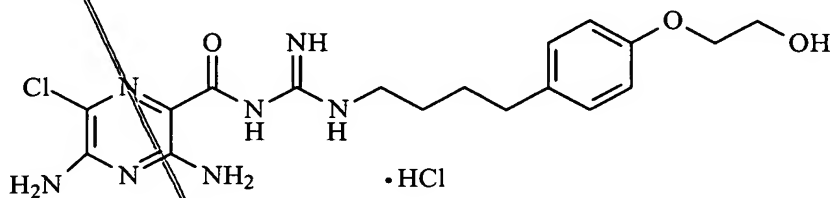


16. The compound of Claim 14, which is represented by the formula:

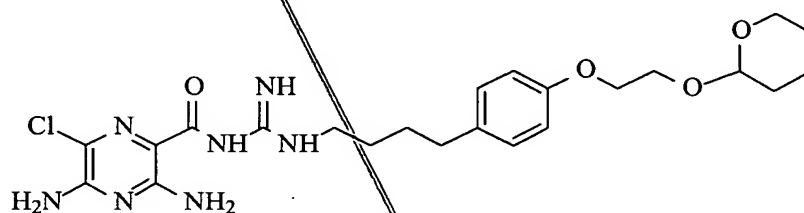


17. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m-OR^8$.

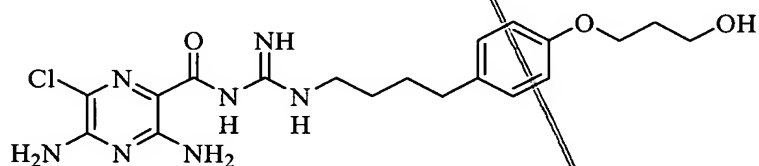
18. The compound of Claim 17, which is represented by the formula:



19. The compound of Claim 17, which is represented by the formula:



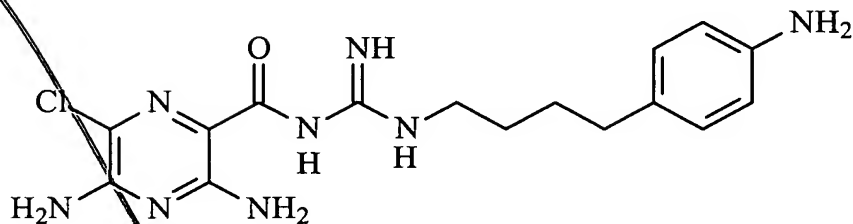
20. The compound of Claim 17, which is represented by the formula:



21. The compound of Claim 13, wherein R^5 is $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$.

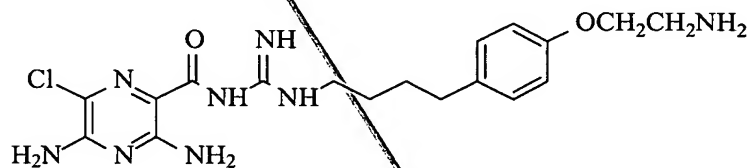
22. The compound of Claim 21, which is represented by the formula:

Q1
Cont

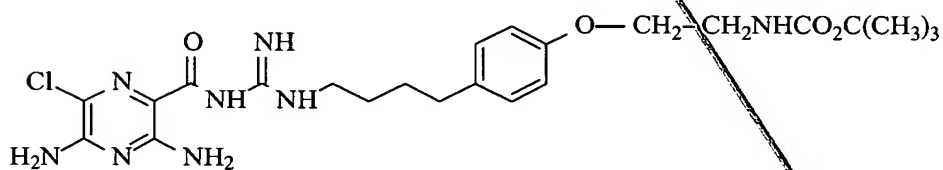


23. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m-NR^7R^{10}$.

24. The compound of Claim 23, which is represented by the formula:



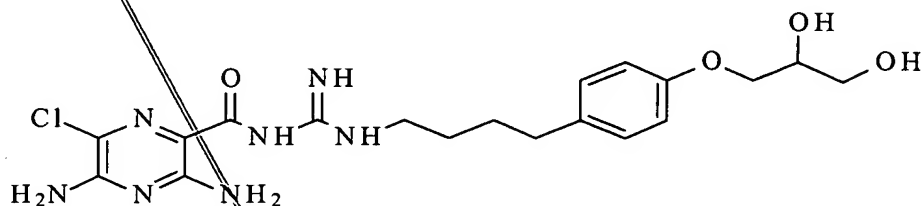
25. The compound of Claim 23, which is represented by the formula:



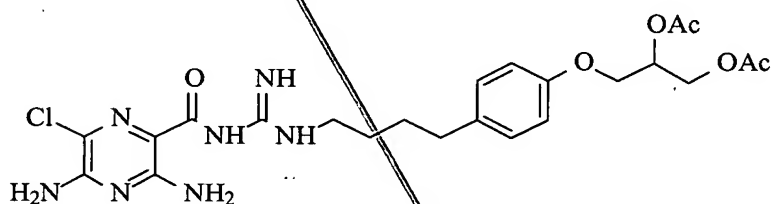
26. The compound of Claim 13, wherein R^5 is $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$.

27. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$.

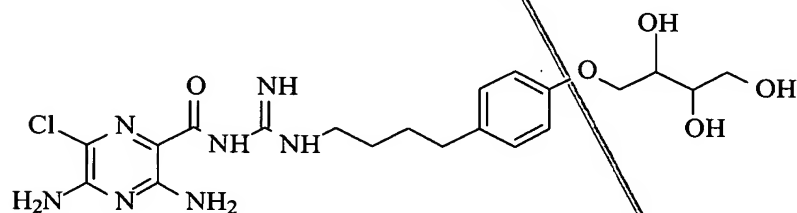
28. The compound of Claim 27, which is represented by the formula:



29. The compound of Claim 27, which is represented by the formula:

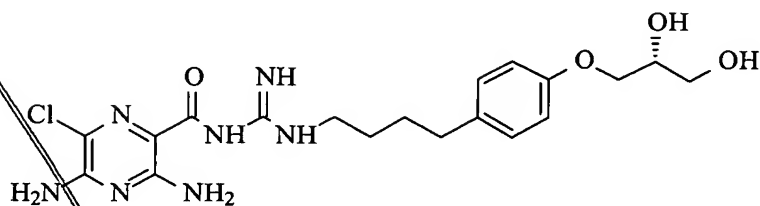


30. The compound of Claim 27, which is represented by the formula:

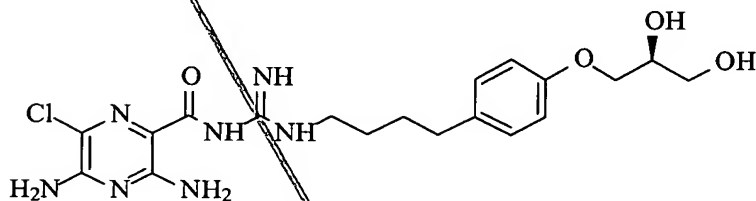


31. The compound of Claim 27, which is represented by the formula:

Q1
Cont



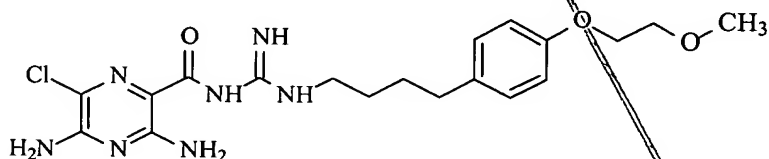
32. The compound of Claim 27, which is represented by the formula:



33. The compound of Claim 13, wherein R^5 is $-(CH_2CH_2O)_m-R^8$.

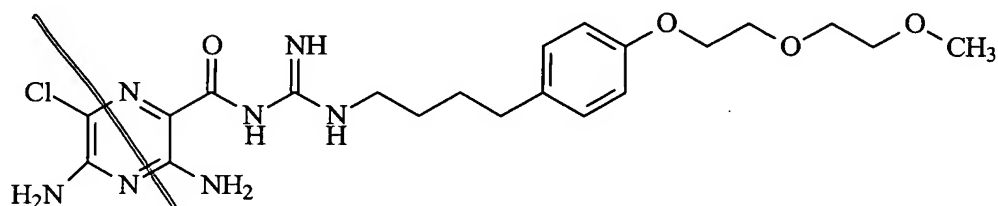
34. The compound of Claim 13, wherein R^5 is $-O-(CH_2CH_2O)_m-R^8$.

35. The compound of Claim 34, which is represented by the formula:

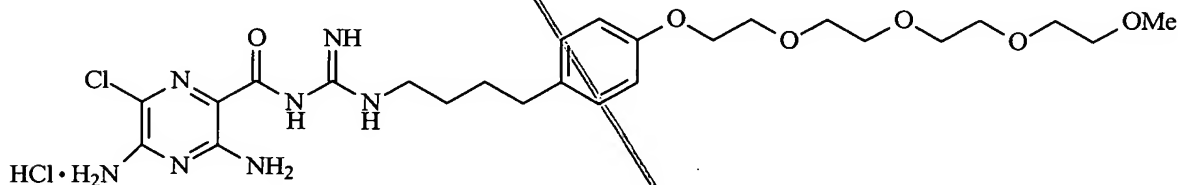


36. The compound of Claim 34, which is represented by the formula:

Q1
Cont



37. The compound of Claim 34, which is represented by the formula:



38. The compound of Claim 13, wherein R^5 is $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$.

39. The compound of Claim 13, wherein R^5 is $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$.

40. The compound of Claim 13, wherein R^5 is $-(CH_2)_n-C(=O)NR^7R^{10}$.

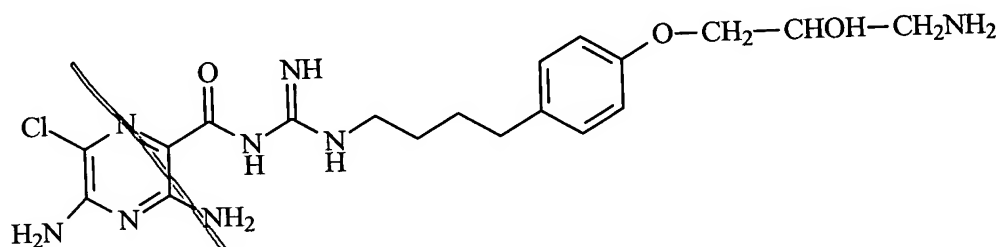
41. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m-C(=O)NR^7R^{10}$.

42. The compound of Claim 13, wherein R^5 is $-(CH_2)_n-(Z)_g-R^7$.

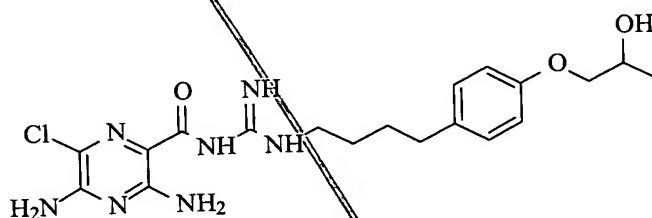
43. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m-(Z)_g-R^7$.

44. The compound of Claim 43, which is represented by the formula:

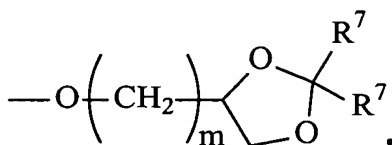
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45. The compound of Claim 43, which is represented by the formula:

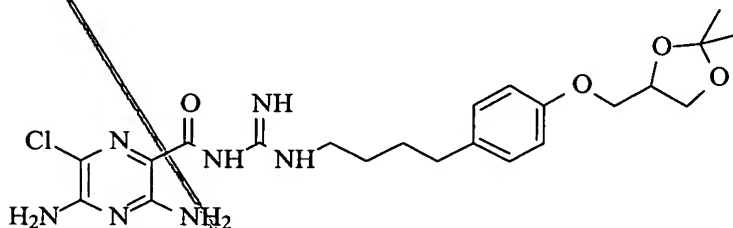


46. The compound of Claim 13, wherein R^5 is $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)$
 $(CHOR^8)_n-CH_2OR^8$.
47. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)$
 $(CHOR^8)_n-CH_2OR^8$.
48. The compound of Claim 13, wherein R^5 is $-O-(CH_2)_m-CO_2R^7$.
49. The compound of Claim 13, wherein R^5 is $-OSO_3H$.
50. The compound of Claim 13, wherein R^5 is $-O$ -glucuronide.
51. The compound of Claim 13, wherein R^5 is $-O$ -glucose.
52. The compound of Claim 13, wherein R^5 is

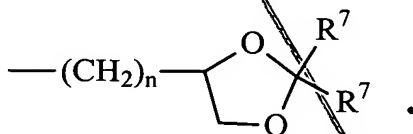


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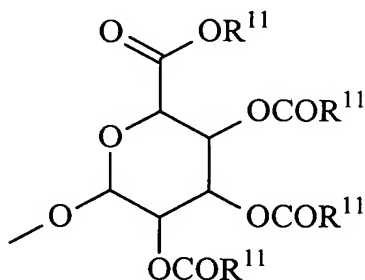
53. The compound of Claim 52, which is represented by the formula:



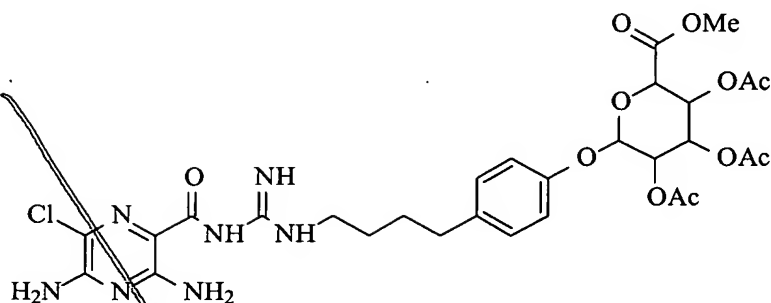
54. The compound of Claim 13, wherein R^5 is



55. The compound of Claim 13, wherein R^5 is



56. The compound of Claim 55, which is represented by the formula:



57. The compound of Claim 1, wherein

X is halogen;

Y is $-N(R^7)_2$;

R^1 is hydrogen or C_1 - C_3 alkyl;

R^2 is $-R^7$, $-(CH_2)_m-OR^8$, or $-(CH_2)_n-CO_2R^7$;

R^3 is a group represented by formula (A); and

R^4 is hydrogen, a group represented by formula (A), or lower alkyl;

58. The compound of Claim 57, wherein

X is chloro or bromo;

Y is $-N(R^7)_2$;

R^2 is hydrogen or C_1 - C_3 alkyl;

at most three R^6 are other than hydrogen as defined above;

at most three R^L are other than hydrogen as defined above; and

at most 2 Q are nitrogen atoms.

59. The compound of Claim 58, wherein Y is $-NH_2$.

60. The compound of Claim 59, wherein R^4 is hydrogen;

at most one R^L is other than hydrogen as defined above;

at most two R^6 are other than hydrogen as defined above; and

at most 1 Q is a nitrogen atom.

61. The compound of Claim 1, wherein R^5 is $-(CH_2)_m-OR^8$.
62. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m-OR^8$.
63. The compound of Claim 1, wherein R^5 is $-(CH_2)_n-NR^7R^{10}$.
64. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m-NR^7R^{10}$.
65. The compound of Claim 1, wherein R^5 is $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$.
66. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$.
67. The compound of Claim 1, wherein R^5 is $-(CH_2CH_2O)_m-R^8$.
68. The compound of Claim 1, wherein R^5 is $-O-(CH_2CH_2O)_m-R^8$.
69. The compound of Claim 1, wherein R^5 is $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$.
70. The compound of Claim 1, wherein R^5 is $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$.
71. The compound of Claim 1, wherein R^5 is $-(CH_2)_n-C(=O)NR^7R^{10}$.
72. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m-C(=O)NR^7R^{10}$.
73. The compound of Claim 1, wherein R^5 is $-(CH_2)_n-(Z)_g-R^7$.
74. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m-(Z)_g-R^7$.
75. The compound of Claim 1, wherein R^5 is $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$.

Q1
Cont

76. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)$
 $(CHOR^8)_n-CH_2OR^8$.

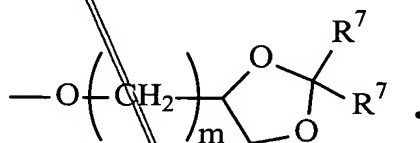
77. The compound of Claim 1, wherein R^5 is $-O-(CH_2)_m-CO_2R^7$.

78. The compound of Claim 1, wherein R^5 is $-OSO_3H$.

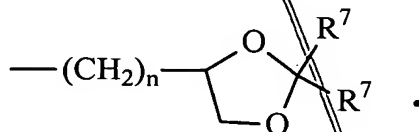
79. The compound of Claim 1, wherein R^5 is $-O$ -glucuronide.

80. The compound of Claim 1, wherein R^5 is $-O$ -glucose.

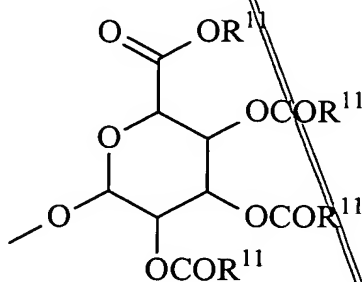
81. The compound of Claim 1, wherein R^5 is



82. The compound of Claim 1, wherein R^5 is



83. The compound of Claim 1, wherein R^5 is



84. The compound of Claim 1, wherein x is a single bond.

85. The compound of Claim 1, which is in the form of a pharmaceutically acceptable salt.

86. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

87. A method of promoting hydration of mucosal surfaces, comprising:
administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

88. A method of restoring mucosal defense, comprising:
topically administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject in need thereof.

89. A method of blocking sodium channels, comprising:
contacting sodium channels with an effective amount of the compound of Claim 1.

90. A method of treating chronic bronchitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

91. A method of treating cystic fibrosis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

92. A method of treating sinusitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

93. A method of treating vaginal dryness, comprising:

Q1
cont
administering an effective amount of the compound of Claim 1 to the vaginal tract of a subject in need thereof.

94. A method of treating dry eye, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject in need thereof.

95. A method of promoting ocular hydration, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject.

96. A method of promoting corneal hydration, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject.

97. A method of promoting mucus clearance in mucosal surfaces, comprising:
administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

98. A method of treating Sjogren's disease, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

99. A method of treating distal intestinal obstruction syndrome, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

100. A method of treating dry skin, comprising:
administering an effective amount of the compound of Claim 1 to the skin of a subject in need thereof.

101. A method of treating esophagitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

102. A method of treating dry mouth (xerostomia), comprising:
administering an effective amount of the compound of Claim 1 to the mouth of a
subject in need thereof.

103. A method of treating nasal dehydration, comprising:
administering an effective amount of the compound of Claim 1 to the nasal passages
of a subject in need thereof.

104. The method of Claim 103, wherein the nasal dehydration is brought on by
administering dry oxygen to the subject.

105. A method of preventing ventilator-induced pneumonia, comprising:
administering an effective amount of the compound of Claim 1 to a subject on a
ventilator.

106. A method of treating asthma, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

107. A method of treating primary ciliary dyskinesia, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

108. A method of treating otitis media, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

109. A method of inducing sputum for diagnostic purposes, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

110. A method of treating chronic obstructive pulmonary disease, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

111. A method of treating emphysema, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

112. A method of treating pneumonia, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

113. A method of treating constipation, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

114. The method of Claim 113, wherein the compound is administered orally or via a
suppository or enema.

115. A method of treating chronic diverticulitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

116. A method of treating rhinosinusitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

117. A composition, comprising:
the compound of Claim 1; and
a P2Y2 inhibitor.

Q1
Cont

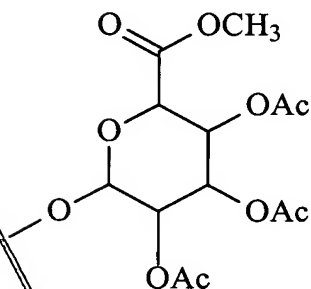
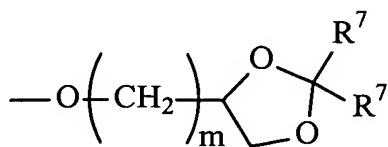
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$$-\text{O}-(\text{CH}_2)_m-\begin{array}{c} \diagup \\ | \\ \text{C}-\text{O}-\text{C}(R^7)_2 \\ | \\ \text{C}-\text{O}-\text{C}(R^7)_2 \\ | \\ \text{C} \end{array}$$
COC(=O)C1OC(OC)C(OC)C1OC(=O)C

-92-

al
cont

and
para



121. The compound of Claim 119, wherein
X is chloro or bromo;
Y is $-N(R^7)_2$;
 R^1 is hydrogen or C_1 - C_3 alkyl;
 R^2 is hydrogen or C_1 - C_3 alkyl;
 R^3 is a group represented by formula (A); and
 R^4 is hydrogen, a group represented by formula (A), or lower alkyl;
at most three R^6 are other than hydrogen as defined above;
at most three R^L are other than hydrogen as defined above; and
at most 2 Q are nitrogen atoms.

122. The compound of Claim 121, wherein
 R^4 is hydrogen;
at most one R^L is other than hydrogen as defined above;
at most two R^6 are other than hydrogen as defined above; and
at most 1 Q is a nitrogen atom.

A'
cont

123. The compound of Claim 120, wherein

X is chloro or bromo;

Y is $-N(R^7)_2$;

R^1 is hydrogen or C_1 - C_3 alkyl;

R^2 is hydrogen or C_1 - C_3 alkyl;

R^3 is a group represented by formula (A); and

R^4 is hydrogen, a group represented by formula (A), or lower alkyl;

at most three R^6 are other than hydrogen as defined above;

at most three R^L are other than hydrogen as defined above; and

at most 2 Q are nitrogen atoms.

124. The compound of Claim 123, wherein

R^4 is hydrogen;

at most one R^L is other than hydrogen as defined above;

at most two R^6 are other than hydrogen as defined above; and

at most 1 Q is a nitrogen atom.

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